# **Original Article**

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# Evaluation of The Role of Transrectal Fine Needle Aspiration As A Diagnostic Modality in The Diseases of Prostate with Review of Literature

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#### **ABSTRACT**

**Introduction:** Transrectal fine needle aspiration cytology is feasible, reliable and highly sensitive diagnostic tool for the diagnosis of prostatic diseases. It mostly involves the elderly men, whose population is increasing in our country with the demographic shift of longitude.

Aims and Objectives: To evaluate the sensitivity, specificity and positive productive value of transrectal fine needle aspiration cytology in addition to other advantages so that it could be accepted as a primary screening tool in the selection of the patients for biopsy and treatment of prostatic lesions.

Material and Methods: Transrectal FNAC was performed in 49 patients, in clinically diagnosed cases of prostate diseases. Histomorphology was also carried out.

**Results:** Satisfactory smears could be obtained in 93.9% cases on first aspiration. The diagnostic accuracy for inflammatory disease was highest (100.0%), followed by malignant (88.8%), and benign lesions (82.9%), with a positive predictive value of 100.0% for malignancy of the prostate. False positivity was seen in 2.09% and false negativity in 11.2% cases.

**Conclusions:** Transrectal FNAC is an accurate, sensitive, highly specific procedure with a high positive predictive value with negligible complication with an additional advantage of possible assessment of prognosis.

**Keywords:** Transrectal FNAC, Franzen Technique, Prostatic Carcinoma.

#### Introduction

Transrectal fine needle aspiration is very quick safe, feasible, atraumatic, highly accurate and economical procedure with negligible complication for the diagnosis of prostate disease, particularly the malignancy. A précised area is required for aspiration; further it does not require anesthesia or any bowel preparation. Therefore it can easily be carried out in the out-patients department of a hospital and in a private clinic.

Ferguson introduced an intraperineal prostatic aspiration technique, which was riddled with many complications.<sup>1</sup> Later Franzen et al evolved a refined technique by adopting a transrectal approach, with a self- made instrument, Kifa syringe to make the procedure safer.<sup>2</sup> Later, Esposti, Zajicek, Ekman et al and Alfthan et al utilized this technique and advocated its reliability, safety, sensitivity, specificity and other advantages as compared to intraperineal FNAC and biopsy.<sup>3-6</sup>

But for the next two decades it was not much accepted in the United States. Klnie and Kannan in 1977 found excellent results of the Franzen technique.<sup>7</sup> India was sluggish in

accepting this procedure, on account of reluctance on the part of general pathologists and lack of experience of the clinician and urologist. Hence very few reports are available from India till end of the 20<sup>th</sup> century.

## **Material and Methods**

This collaborative study was performed in the departments of Surgery and Pathology of JN Medical College, AMU, Aligarh on 49 patients of provisionally diagnosed cases of prostatic disease with the help of a lumber puncture needle of 22/23G. Fine needle aspiration cytology was performed by the Franzen technique from hard and nodular areas of the prostate. In each case 2-5 passes per aspiration were carried out and total material obtained was spread on 3-4 grease free slides. All the slides, which were for Pap and H and E staining were immediately fixed in 95% alcohol except one which was air dried for MGG stain. Cytological diagnosis was based on the criteria laid down by Koss.8 Histopathological tissue was obtained by trucut biopsy or excision of the prostate. Paraffin blocks were prepared of the tissue after fixation in 10% formalin. 3-5µ thick sections were cut and stained with VG stain. Histopathological

tissue was obtained in 44 cases and its correlation with cytology could be done in 40 cases only.

#### **Observations**

In our study, the youngest patient was 25 years old and the oldest was 85 years of age, with the mean age of 59.16 years. Clinically most of the patients presented with features of prostatism. There was increased frequency of micturition in 75.0%, followed by acute retention of urine in 73.5%, thinning of urinary stream in 65.3%, hesitancy in 55.6%, urgency in 42.0% and haematuria in 12.2% patients.

The clinical grading by per rectal examination revealed grade III enlargement of prostate in 23 cases (46.9 %), grade II in 18 cases (40.8%) and grade I in 8 cases (14.3%). The rectal mucosa was mobile in 47 (95.5%) cases and fixed in 2 (4.1 %) cases. In grade III cases, the surface of prostate was smooth with firm consistency in 15 cases, and hard and nodular in 8 cases. In grade II cases, the surface was smooth with firm consistency in 13 cases and hard and nodular in 5 cases. All the cases of grade I had smooth surface, with soft to firm consistency. (Table 1)

Out of the 32 clinically diagnosed benign lesions, 26(81.3%) were found to be benign and 1 (3.1%) each malignant, suspicious of malignancy and inflammatory while 3 (19.4%) cases were unsatisfactory on cytological examination. Among the 8 clinically diagnosed malignant cases, 7(87.5%) were found to be malignant and 1(12.3%) benign on cytological examination. Smears from malignant cases showed cohesive clusters and sheets of highly atypical cells with marked anisocytosis and anisonucleosis, with

overlapping of nuclei and crowding, with acinar formation at places (Figure 1 and 2). The 4 cases of inflammation were found to be suffering from prostatitis. The rest of the 5 cases which were clinically highly suspicious of malignancy revealed 3(60.0%) as benign and 1 each (20.0%) as malignant and highly suspicious of malignancy on cytological examination. (Table 2)

Out of the clinically diagnosed 49 cases of prostatic diseases, 35(71.4%) cases were diagnosed as benign and 9(18.4%) cases as malignant on histopathological examination. Out of the remaining 5 cases, 4 were already confirmed on FNAC as prostatitis and 1 did not allow any surgical procedure. Out of the 5 cases highly suspicious of malignancy clinically, 1(20.0%) was malignant and 4(80.0%) benign on histopathology. (Table 3)

The overall diagnostic accuracy was 85.4% in our study. The diagnostic accuracy in malignancy was 88.8% with a false negative rate of 11.1% in our study. In the benign lesions, the diagnostic accuracy was 82.9% with false negative rate of 11.2% and false positive rate of 2.9%. (Table 4) The unsatisfactory smears were 6.2%. The clinically diagnosed 13 cases of malignancy including the suspicious cases, revealed a sensitivity of 88.9% and specificity of 100.0% on FNAC. In the clinically diagnosed 32 patients of benign hypertrophy, FNAC showed a sensitivity 92.9% and specificity of 75.5%. The statistical analysis showed a positive predictive value of 100.0% in malignancy and 92.3% in benign prostatic hypertrophy on FNAC. A negative predictive value was 80.0% in malignant disease and 60.0% in the benign disease in our study. (Table 5)

Table I: Correlation of Cytological and histopathological diagnosis of the clinical grades of enlarged prostate.

Grade III Enlarged prostate	Smooth, Firm and closed	Diag	ВРН	Suspicious of malignancy	Malignant	Prostate	Unsatisfied	Total
		Cyto	12	-	11	1	-	
		Histo	12+1	-	11	-	-	15
	Hard & Nodular	Cyto	3	1	4	-	-	
		Histo	3+1	-	4	-	-	8
Grade II Enlarged prostate	Smooth & firm	Cyto	9	-	1	-	3	
		Histo	9+3	-	1	-	-	13
	Hard and Nodular	Cyto	3+1	-	1	-	-	
		Histo	3	-	11	-	-	5
Grade I Enlarged prostate	Smooth and Soft	Cyto	2	1	1	4	-	
		Histo	2+1	-	-	-	-	8

Table 2: Correlation of Clinical and Cytopathological Diagnosis.

Clinical Diagnosis	Total No of Cases	Cytopathological Diagnosis						
		Benign (%)	Malignant (%)	Inflammatory (%)	Suspicious of malignancy (%)	Unsatisfactory (%)		
Benign	32	26(81.3)	1(3.1)	1(3.1)	1(3.1)	3(19.4)		
Malignant	8	1(12.3)	7(87.5)	-	-	=		
Inflammatory	4	-	-	4(100)	-	=		
Suspicious of Malignancy	5	3(60)	1(20)	-	1(20)	-		
Total	49	30	9	5	2	3		

Table 3: Correlation of Clinical and Histopathological Findings.

Clinical Diagnosis	Total No of Cases	Histopathologic Impression				
Clinical Diagnosis	Total No of Cases	Benign (%)	Malignant (%)	Inflammatory (%)		
Benign	32	31(96.9)	-	1(3.1%)		
Malignant	8	-	8(100)	-		
Inflammatory	4	-	-	4(100)		
Suspicious of Malignancy	5	4(80)	1(20)	-		
TOTAL	49	35	9	5		

Table 4: Comparative diagnostic accuracy of FNAC and Biopsy in Carcinoma of Prostate.

Authors	Year	Total No. of cases	Diagnostic Accuracy on FNAC	Diagnostic Accuracy on Biopsy	
Esposti	1974	350	97.0	96.0	
Ekman	1967	100	90.0	90.0	
Alfthan et al	1970	220	95.0	88.0	
Epstein	1976	118	86.4	85.6	
Kline& Kannan	1982	540	92.0	88.6	
Hermida et al	2001	58	94.0	93.0	
Saleh et al	2005	60	91.7	88.0	
Pantola et al	2012	78	95.2	89.7	
Our Study		49	88.8	85.4	

Table 5: Evaluation of Trans-rectal FNAC in Prostatic Carcinoma with Statistical Correlation.

Authors	Year	Total No. of Cases	Cyto- histological correlation (%)	Sensitivity (%)	Specificity (%)	False Negative (%)	False Positive (%)
Ekman	1967	100	76.0	90.0	80.0	7.2	2.0
William et al	1967	51	76.0	96.0	100	4.0	0
Alfthan et al	1970	220	88.0	95.0	96.5	6.4	1.4
Lin et al	1972	27	71.0	81.5	100	5.0	0
Kline & Kannan	1982	416	87.0	88.0	91.0	12.0	8.0
Melagrana et al	1982	87	80.0	80.0	92.0	20.0	9.0
Mondal et al	1990	126	98.4	98.4	100	1.6	0
Hermida et al	2001	497	96.0	96.0	96.0	4.0	2.0
Saleh etal	2005	60	91.7	88.0	93.0	4.8	7.5
Tariq et al	2007	56	93.0	94.0	96.0	3.3	0
Pantola et al	2012	121	95.2	98.7	98.7	4.8	1.6
Reddy and Rani	2016	27	84.2	84.0	97.0	3.2	4.2
Our Study		49	96.7	90.9	87.8	11.2	2.9

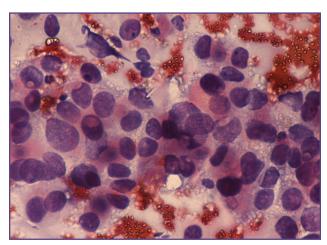


Fig. 1: Fine needle aspiration cytology of the prostatic mass showed cohesive clusters of highly atypical cells with marked anisocytosis and anisonucleosis, with acinar formation at places. Haematoxylin and Eosin x 40X.

### **Discussion**

A better health care system is available now all over the world. Gawandi reported in his recent book," Being MORTAL" that progress in medicine and public health is an incredible boon and people live long. Unfortunately in India prostatic diseases in elderly men is increasing with the demographic shift of longevity.

The incidence of carcinoma of the prostate and its mortality rate varies worldwide. <sup>10,11</sup> In UK it is the sixth most common neoplasm. <sup>12</sup> In USA alone, it is the third most common cause of cancer death in males. <sup>13,14</sup> From USA and Australia, it has been reported to cause 20% morbidity and 11-20% mortality. <sup>13,14</sup> Later Joseph and Fajers reported carcinoma prostate to be the second leading cause of cancer death. <sup>15</sup> In Iraq, it was registered to be one of the commonest among the ten cancers in males. <sup>15</sup> Korean report shows a recent increase in the incidence of cancer prostate. <sup>16</sup>Prostatic cancer is presently the fifth most common newly diagnosed malignancy in Korean men. <sup>17</sup> The incidence India is reported as 6.8 per one lac, which is increasing now. <sup>18</sup>

The age group involved in the west is mostly 7<sup>th</sup> or 8<sup>th</sup> decade, while in India, most of the cases are seen in the 6<sup>th</sup> decade of life. <sup>13,19</sup> In our study, the average age of the patients was 59.2 years, findings similar to Mandhani and Reddy & Rani. <sup>18,19</sup> The difference of age of affliction between India and the west can easily be explained on the basis of shorter life span in India as compared to the west. Scadino et al found on autopsy of elderly men between 75- 93 years, that occult carcinoma unclinically diagnosed was found in 80.0% cases over the age of 80 years. <sup>20</sup> They

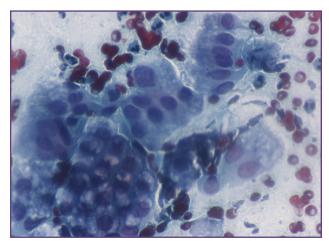


Fig. 1: Fine needle aspiration cytology of the prostatic mass showed cohesive clusters of highly atypical cells with marked anisocytosis and anisonucleosis, with acinar formation at places. Haematoxylin and Eosin x 40X.

further observed that autopsy cases included one-fifth potentially malignant tumors, which on manifestation could have been fatal. But four-fifth would have remained as occult carcinoma. This indicates that early detection of cancer prostate is of paramount importance, as it may be curative, like cervical cancers in females. The most common clinical presentation in our study was increased frequency of micturition, followed by acute retention of urine; these findings are comparable to reports of Reddy and Rani.<sup>19</sup>

Early detection of prostate cancer requires a frequent and skillful digital rectal examination (DRE), with a high index of suspicion for the induration and nodules.<sup>21</sup> Thirteen out of 49 cases in our study were found to have hard and nodular prostate on digital rectal examination (DRE). Among these, 7 were found malignant but only 6 (46.7%) could be confirmed by biopsy. Similarly Jewett in 211 cases and Goodwin in 301 cases on DRE could demonstrate the presence of malignancy on aspiration in 57.0% and 50.0% cases respectively.<sup>22,23</sup> The hard and nodular prostate is one of the foremost clinical manifestation of cancer, but it may not be pathognomonic of malignancy in every case. 22,23 Later with more experience in the technique and better knowledge of the criteria of malignancy in fine needle aspiration cytology, Mondal et al and Tariq et al could diagnose 96.0% and 93.0% cases on DRE respectively. 24,25

Planelles et al and Gomez et al observed the presence of malignant cells in FNAC of all the 72 (100%) cases suspicious of malignancy on DRE, with PSA levels 20-30μg/ml.<sup>26,27</sup> Reddy and Rani could diagnose only 84.0% of their 27 cases on DRE.<sup>19</sup> They reported a high false negative report of 15.8%, which probably may be the

reason for low diagnosis. This can be suggested that cases with induration and nodulation on DRE with suspicion of malignancy can help in the selection of patients for FNAC and core biopsy. We can affirm by our long experience of four decades in cytopathology that if malignant cells are seen in the smears, then confirmation by biopsy is not a necessity. Ekman et al also emphasized that a positive cytological diagnosis of cancer should be regarded as unequivocal evidence of a malignant growth.<sup>5</sup> Suhrland et al and Kher et al also opined that a positive cancer diagnosis by cytology even if not confirmed by biopsy, is still an indication of malignancy of the prostate. 28,29 But a classical biopsy is the final arbitrator for doubtful or suspicious cases.<sup>28,29</sup> Although a classical biopsy is the final arbitrator for doubtful or suspicious cases, Johnson & Fajers, Hock et al and Wahi tried to evaluate cytological diagnosis of smears of prostatic secretions obtained by massage, in search of early detection of cancer prostate, with a success of 61-81%. 15,30,31 Prof Wahi emphasized this technique as a method of choice, when one of his cases showed malignant cells in the smears of prostatic secretions, with twice negative tissue biopsy, which later was proven after radical resection.31

Although this smear technique found optimism, but later it was found unsuitable for the diagnosis of prostate malignancy as compared to the classical reliable histomorphological study of incisional and excisional biopsy. The perineal and transrectal biopsies of the prostate claimed to provide better results. 16,21 But perineal and transrectal biopsies were plagued with multiple complications.<sup>21,24</sup> Anderson et al combined the transrectal biopsy by a large bore needle (veenema) in 379 cases with transrectal fine needle aspiration in 69 cases.<sup>32</sup> They reported complications of biopsy like haemorrhage, deep vein thrombosis and febrile illness in 19.5% cases. Puigvert et al found perineal tumor implantation following needle biopsy of prostatic masses with large bore needles (Turkle, Vim Silverman Needle, Veenema, Malinger, Blanchard).33 Ekman et al in 100 cases and Alfthan et al in 220 cases reported no complications of transrectal biopsies.<sup>5,6</sup> But Bissada et al and Thompson et al found it responsible for high frequency of infections. 34,35 Volter and Zeiglar reported fever as high as 39°C for 12 days in 9(0.9%) cases and bloody urine in 15 (1.5%) in a total of 1020 cases studied by transrectal aspiration.36

Eaton performed blood culture in 20 patients 10 minutes after the transrectal biopsy and found positive in 17(95.0%) cases.<sup>37</sup> Hosking et al obtained blood culture in 19 patients one hour and in 14 patients 5 minutes after

aspiration.<sup>38</sup> Only 2 cases out of 33 were found to be positive for staphyllococcus epidermidis.<sup>38</sup> This suggested that transrectal FNAC even without bowel preparation or antibiotics does not cause bacteremia.

In search of early detection of prostate carcinoma, surgery on a normal elderly person was a real tragedy. Therefore improvement in diagnostic tool as franzen transrectal aspiration was a real boon. It was found to be feasible, reliable, quick, easy, less traumatic and safe with high diagnostic accuracy, ranging from 90-96%, with an experience of 20 years in transrectal aspiration.3 The comparative study of diagnostic accuracy of fine needle aspiration and core biopsy in carcinoma prostate showed a higher diagnostic accuracy of FNAC as compared to biopsy in our study. Al-Ababi compared the results of cytology and histology and found that the sensitivity of fine needle aspiration was 98.0% as compared to core biopsy sensitivity of 96.0% in carcinoma prostate.<sup>39</sup> Similar observations have been reported by Ekman et al, Alfthan et al, Kline et al, Tariq et al, Al Ababi, Narayan et al, M Cho et al, Ljung et al, Chodak et al, Deliveliotis et al, Carter, Pantola et al and Saleh et al.5-7,25,39-47 But our results were contradictory to the study of William and Ou et al. 48,49

The evaluation of transrectal FNAC in prostatic carcinoma in our study showed a sensitivity of 88.8%, which is comparable to the findings by Saleh et al and Kaur et al, who have reported it to be 88.0% and 90% respectively. 47,50 Our study showed a positive predictive value of 100.0% in malignancy and 92.3% in benign prostatic hypertrophy on FNAC. Pantola in their 121 cases reported positive predictive value of 97.6% and negative predictive value of 97.5%, with a sensitivity of 95.2%. 46 Hermida et al in their 497 cases showed a positive predictive value of 91.0% and negative predictive value of 93.0 with 96% sensitivity.14 Bently et al in their 170 cases found sensitivity of 88.0% and positive predictive value of 78.8%.<sup>51</sup> The positive predictive value is the probability that the patient had the disease, when the test was called positive, but a negative predictive value indicates that the patient is disease free. The predictive values (PV) are dependent on the criteria and prevalence of malignancy in the population. Thus PV are an aid to the urologists in deciding as to what importance should be assigned to the reported results. These reports help the urologists in making the clinical decisions, based on the FNAC findings provided by the cytopathologists. It has been observed that the clinicians experience with expertise in Franzen technique and interpretation of the cytological findings will be a real help in the medical care of the patients.

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The efficiency is the frequency with which all cases are correctly classified as malignant or benign. Although it is accepted that FNAC by franzen technique gives excellent results by the combination of a clinician and a competent pathologists, still some limitations in the form of false negative and false positive diagnosis have been observed.<sup>28,45</sup> False negative diagnosis in our study 11.2% which was equivalent to Kline and Kannan and Ingle and Ingle, who reported 12.0% and 12.8% respectively.<sup>7,10</sup> Melagrana et al and Lin et al reported higher false negative cases as 20.0% and 29.0% respectively.<sup>52,53</sup> As most of the clinicians are aware of the hazards which is inherent, mostly on account of insufficient smears and are always prepared to repeat the aspiration, if they clinically suspect malignancy. Further it can be confirmed on long follow up, on repeat aspiration. The false positive diagnosis is more a hazard in cytologic preparations, which may be due to misinterpretation of atypical cells. Further it could be due to contamination from rectal mucosa, dysplasia and therapy induced alterations.<sup>51</sup> Cytodiagnosis can be improved by the collection of sufficient material, which is possible with larger number of passes per aspiration. Besides, more material can be obtained from the peripheral part of tumor which is soft and cellular as compared to the hard center. Multiple passes are not possible with biopsy needle. Insufficiency report varies from 1.3-6.4% in most of the studies. 48,54 Our insufficiency in the total 49 cases was only 6.2%. Melagrana after repeat aspiration could increase sensitivity of carcinoma cases from 77.0% to 80.0%.52

In cytology the borderline cases between benign atypia and malignancy in cell groups is difficult to interpret.<sup>55</sup> The problem of whether these false positive reports are in fact due to small malignancies or due to misinterpretation of atypical prostate cells, can be only answered by long term follow up or repeat aspiration with additional use of imprint cytology.<sup>55,56</sup> It is noted that lack of knowledge of the special features of atypical hyperplasias, the incidence of which may be upto 49.09% may lead to error in the interpretation.<sup>57,58</sup>

Gaetani and Trentini described the cytomorphological features of atypical hyperplasia of the prostate, which helped the pathologists to differentiate it from poorly differentiated carcinomas.<sup>59</sup> Atypical prostate cell is an abnormal cell, with greater activity than ascribed with certainty to reactive changes.<sup>59</sup> The important features are tumor cell in well spaced clumps in acinar pattern with mild pleomorphism and nuclear moulding disposed on an eosinophilic background of secreted matter, with

a finely granular appearance. This cell disposition was a representative of the histologic pattern of atypical hyperplasia, characterized by acini usually bordered by the pseudostratified undifferentiated epithelial cells, showing severe degree of loss of polarity. Another relevant feature was the lack of RNA, which is more in carcinoma than atypical hyperplastic cells, seen under fluorescent microscope after acridine orange stain.<sup>59</sup>

Koss had described these atypical cells as a group of pluri-stratified plugs of epithelial cells of quasi-papillary appearance with fairly regular nuclei, which may arouse suspicion of malignancy. Gaetani and Trentini were of the opinion that atypical epithelial hyperplasia represents the main pitfall in the cytologic diagnosis of poorly differentiated prostatic carcinoma. These two lesions are characterized by undifferentiated or poorly differentiated carcinoma cells with several features in common, which leads to false positive diagnosis. Poorly differentiated carcinoma cells are disposed as singly or in small groups with non-uniform irregular nucleus with coarse clumped chromatin and large atypical mitotic figures. So

Further the inability to differentiate benign atypia from well differentiated carcinoma was also attributed to low diagnostic accuracy.3 To differentiate well differentiated carcinoma from atypia, Esposti described the former as a microadenoma complex with central cytoplasm and a peripheral nuclei and occasional free cells.3 Later Epstein pointed that acinar arrangement with stratified arrangement of nuclei bore no relationship to well differentiated carcinoma.<sup>57</sup> He further emphasized that the following five features of neoplasisa should be observed for the diagnosis of well differentiated carcinoma: 1) loss of polarity 2) presence of nucleoli 3) anisonucleosis 4) moulding of nuclei and 5) acinar arrangement of cells with hyperchromatic nuclei. Though these studies were conducted in different geographical areas, discussions by Geetani of atypia and critical analysis of Epstein of well differentiated carcinoma, did help in arriving at a concurrent and feasible diagnosis. 59,57

Cytology can be further helped by cell block like biopsy and aided by imprint smear to increase the diagnostic accuracy and sensitivity of the technique. Mohler et al studied the cell block and opined that it can be used as a safeguard against the radical treatment of false positive diagnosis. 60 It may further help the cytologists in improving the diagnostic accuracy, who are familiar with prostatic histopathology. Another advantage of FNAC is the possible assessment of prognosis of cancer prostate,

based on cellular pleomorphism. The grades of cancer as evaluated by pleomorphism are favorably comparable to the histologic grading. Esposti in his study on 469 patients by transrectal fine needle aspiration biopsy cytologically graded prostatic carcinoma on the basis of cell differentiation as well differentiated, moderately differentiated and poorly differentiated.<sup>3</sup> These patients were treated with hormone and the prognostic significance of differentiation grading was evaluated in terms of response to treatment. Diana on her clinico-cytological study on 50 cases of malignancy of prostate showed a stable disease in high cytologic grade and a progressive disease in poorly differentiated grade of cancer.<sup>61</sup>

#### **Conclusions**

FNA cytology is easy, safe, quick and economical technique and can be easily performed in an out-patient clinic by an experienced urologist. The problem of correct diagnosis leading to high sensitivity can now be overcomed by the knowledge of newly supplemented criteria of atypia and well differentiated carcinoma. Further the hurdle of prognosis can be overcome by cytomorphological grading after hormonal treatment with or without orchidectomy by a competent pathologist. Therefore for the diagnosis of prostatic lesions by Franzen's FNAC is an important modality in the armamentarian of the pathologist as well as urologist and should be utilized in primary screening of all prostatic lesions.

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